

Study Protocol

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Title

Ultrasound-guided intermediate cervical plexus block

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Study protocol (Summary)

Title

Ultrasound-guided intermediate cervical plexus block

Introduction

For interventions on the carotid artery both general and regional anesthesia are established anesthetic procedures. The AWMF S3 guideline recommends that you make a selection based on the center-specific experience. Only for patients with contralateral carotid closure regional anesthesia is recommended as gold standard.

Carotid surgery of the awake cooperative patient can be considered the gold standard of neuromonitoring. Critical changes in cerebral blood flow during the clamping phase can be detected immediately, an operative shunt can be applied as needed. Conservative treatment of carotid stenosis includes treatment with anticoagulants (usually aspirin). For this reason, a blockade of the cervical plexus should be performed under ultrasound control. Serious side effects such as an intra-arterial injection of the local anesthetic can be avoided in this way. However, the increased safety of an ultrasound-guided approach is not yet proven in large studies.

The innervation of the carotid triangle is complex and includes cranial nerves (innervation of the vessel wall and neck muscles) as well as portions of the cervical and brachial plexus.

We investigate whether an ultrasound-assisted cervical plexus block in combination with additional subplatysmal application of local anesthetic to the superficial cervical ansa cervicalis (anastomosis between the cervical plexus and the facial branch of the facial nerve) results in high anesthetic quality.

Study design

single-center, prospective

Study goal

anesthetic quality

Health economic goals

We expect that the result will affect puncture technique in ultrasound-guided cervical plexus blocks for carotid surgery.

Interventions

Intervention A	20ml ropivacaine 0.75% (interfascial compartment at the level of the carotid bifurcation)
Intervention B	5ml prilocaine 1% (subplatysmal injection between the medial edge of the sternocleidomastoid muscle and the submandibular gland)
Intervention C	5ml prilocaine 1% (perivascular injection within the carotid sheath)
Intervention D	Supplementary local anesthetic infiltration by the surgeon (prilocaine 1%)

Patient population

Adult men and women undergoing open-surgical carotid desobliteration.

Study center

HELIOS Medical Center Schwerin, Germany

Schedule

12-18 months

1. Introduction

For interventions on the carotid artery both general and regional anesthetics are established anesthetic procedures. Surgery of the awake patient can be considered the gold standard of neuromonitoring.

2. Primary and secondary outcome parameters

With this prospective study design of ultrasound-guided cervical plexus blocks in carotid surgery, we examine whether additional application of local anesthetic to the superficial cervical ansa (anastomosis between the cervical plexus and the cervical branch of the facial nerve) results in complete surgical anesthesia.

The main objective is the quantity and location of the local anesthetic supplementary injected by the surgeon. Secondary outcome parameters are procedure-typical side effects.

We further investigate the effect of perivascular injection inside the carotid sheath on side effects and anesthetic quality.

3. Study design

This is a single-center prospective study.

4. Schedule

The estimated recruitment schedule is approximately 12-18 months.

5. Patient population

5.1. Inclusion criteria

The following inclusion criteria must be met :

- Surgical carotid deobliteration in symptomatic or asymptomatic carotid stenosis
- Age over 18 years
- Written informed consent

5.2. Exclusion criteria

Patients who meet one or more of the following criteria should not be included in the study:

- local as well as systemic signs of inflammation
- comorbidities with the highest risk of anesthesia (ASA risk group V)
- severe arrhythmias in the absence of a pacemaker
- pronounced anemia
- decompensated heart failure
- manifest shock
- known allergy to local anesthetics used
- manifest polyneuropathy
- pregnancy, breastfeeding
- participation in other studies
- non-oriented or non-cooperative patients

- known persistent drug, drug or alcohol abuse

5.3. Co-morbidities

Preexisting co-morbidities are documented in the patient record.

5.4. Co-medication

All medications that are given in addition to the study medication are considered concomitant and are documented in the patient record (especially medications that have an inhibitory effect on the coagulation system).

6. Study protocol

6.1. Recruitment

The patients are recruited in the context of anesthesiological preparation. Patients who have confirmed their participation in the exam by written informed consent will first be clinically evaluated. If the patient meets all inclusion and no exclusion criteria, the patient is enrolled in the study.

6.2. Allocation of the study medication

After admission to the study, each patient will receive a patient number, which will be noted on the Case Report Form (CRF). The decision on the intervention C (5 ml prilocaine 1% perivascular within the carotid sheath) is made by the investigator on the basis of the individual sonoanatomy.

6.3. Monitoring and preoperative preparation

Patients are initially treated in the context of a normal preoperative preparation. This includes the installation of a peripheral venous access with the connection of 1000 ml of electrolyte solution (Jonosteril®) by an anesthesia nurse in the induction room. Thereafter, the radial artery is cannulated on the non-operated side. The following parameters are monitored until complete postoperative recovery:

- Non-invasive blood pressure
- Invasive-arterial blood pressure
- Electrocardiogram
- Pulsoxymetry

The parameters are documented in the anesthesia protocol.

6.4. Interventions

The ultrasound-guided regional anesthesia is performed by one of two experienced anesthesiologists. First, we perform a spray disinfection with octenidine. We use an ultrasound device from Sonosite (EDGE), Bothell, WA, United States, with a linear transducer (HFL38). The puncture is performed with a 24G cannula from Pajunk, Geisingen, Germany, in an in-plane technique.

Intervention A	20ml ropivacaine 0.75% (interfascial compartment at the level of the carotid bifurcation)
Intervention B	5ml prilocaine 1% (subplatysmal injection between the medial edge of the sternocleidomastoid muscle and the submandibular gland)
Intervention C	5ml prilocaine 1% (perivascular injection within the carotid sheath)
Intervention D	Supplementary local anesthetic infiltration by the surgeon (prilocaine 1%)

6.5. Follow-up

Patients are initially cared for in the postoperative anesthesia care-unit (PACU). Depending on the clinical condition of the patients, further care is provided either at the normal ward or on an intensive care unit. For all study patients, a daily clinical visit is made until discharge.

6.7. Health economic assessment

We expect the study to have implications for the practice of ultrasound-guided cervical plexus blocks for carotid surgery. The fundamental goal is the optimization of this regional anesthesia technique.

7. Adverse events

7.1. Adverse events due to the local anesthetic

Allergic reaction

Allergic reactions are very rare in amide-type topical anesthetics and are mostly due to the methylparaben preservative contained in larger packs (e.g., 50ml bottles).

Local Toxicity

There are no major studies on local-toxic effects of prilocaine or ropivacaine. Possible would be a disturbance of the periaxonal milieu or the nervous blood supply (compartment effect of the local anesthetic depot). Neurological complications occurred after hyperbaric lidocaine was continuously administered intrathecally with 7.5% glucose. Similar observations were not made for peripheral nerve blocks.

Systemic Toxicity

Systemic toxicity occurs at high plasma levels by intravascular injection or absolute or relative overdose with rapid resorption of the local anesthetic from the site of action.

The cerebral tendency to seizure is increased by the local anesthetic effect on inhibitory cortical centers. With or without preconvulsive warning signs (numbness of the tongue and perioral, metal taste, slurred speech, ear blades, blurred vision, restlessness), generalized convulsions occur. With rising plasma levels, coma and respiratory paralysis can occur.

Inhibition of intracellular ATP production and blockade of sodium channels (vasal, cardiac, sympathetic) results in hypotension and variable cardiac arrhythmias (bradycardia to asystole, ventricular arrhythmias to ventricular fibrillation).

In a large-scale prospective study by Auroy et al. (Anesthesiology 1997) in more than 100,000 regional anesthesia, the risk of serious complications was stated as follows: cardiac arrest 3.1 / 10000, case of a convulsion 2.2 / 10000; Death 0.7 / 10000.

7.2. Adverse events due to the peripheral nerve block

Complications may be due to needle trauma (vascular or nerve lesion), local infection or as a result of improper storage on the operating table (pressure lesion). Long-term neurological damage was reported in 0.19% to 1.7% depending on the examination, with various possible causes (nerve block, surgery, storage) being subsumed here.

In addition - usually not serious - complications may occur in connection with the unfamiliar stress situation of the surgical procedure: vagovasal syncope or anxiety with hypertensive circulatory regulation.

7.3. Evaluation of adverse events

Prilocaine and ropivacaine are drugs approved for peripheral nerve blocks that we use within the maximum permitted dose and indication. All occurring complications are documented and the likelihood of the causal relationship with the regional anesthesia procedure is stated. Since this is a standard regional anaesthesia procedure, it can not be expected that previously unknown complications will occur.

7.4. Information to the ethics committee

In accordance with the GCP Regulation, any severe adverse event (SAE) or unexpected (SUSAR) adverse event occurring during the trial that could affect the safety of the subjects or the conduct of the trial will be reported to the relevant local ethics committee. The report is issued by the head of the clinical trial.

Non-serious adverse events are documented on the appropriate adverse events page in the Patient Documentation Sheet (CRF) and in the patient's medical record.

8. Dropout of patients

The non-therapy-related reasons for dropout from the study include in particular the revocation of consent by the patient. In addition, exclusion of the patient may result if the investigators subsequently become aware of exclusion criteria (e.g., pregnancy or participation in another clinical trial).

Dropout reasons are documented as therapy-related if they make the surgical procedure impossible in connection with acute complications. These include e.g. severe cardiovascular complications (cardiac arrest, shock, threatening arrhythmias) due to the systemic toxicity of the local anesthetic.

In case of incomplete nerve block, it is supplemented by the surgeon with prilocaine 1%. Quantity and place of application are documented and the procedure is carried out as planned without excluding the patient from the study. Conversion of the anesthesia procedure (induction of general anesthesia) is also documented in the CRF.

9. Statistical Analysis

The statistical test methods are described in the statistical analysis plan. The starting point is the assumption that the examined characteristics are not normally distributed. The evaluation is done in cooperation with a statistician (www.p-wert.de).

10. Data management

The investigator is responsible for the correct and complete input of patient data in the case report form (CRF). The CRF is deposited for at least 15 years together with a copy of the anesthesia protocol and surgical report. In the case of a data transfer (statistical analysis, publication of the data) only the patient number is forwarded, thus preserving the privacy of the patient. A later identification is possible by depositing the patient identification list in the examiner.

The patient provide written informed consent on the evaluation and transfer of his data. The original of this protocol will be deposited in the examiner, a copy is given to the patient.

11. Ethical, legal and administrative aspects

The investigator ensures that the test is performed in accordance with existing laws and regulations (ICH and GCP Guidelines, AMG). The study protocol and patient information are submitted to the Ethics Committee of the University of Rostock.

Before starting the study, each patient must give written consent to the investigator, having previously been fully informed in an understandable manner about the nature, significance and scope of the clinical trial. The content of this information is documented on the consent form. The patient will be given a copy of the signed consent form. The investigator copies the original of the consent form in the investigator folder.

Carrying out a nerve blockade for carotid surgery is routine clinical practice. Thus, subjects and investigator are covered by the liability insurance of the HELIOS Medical Center Schwerin. The Liability Insurance Company was informed by the "Safety Department" about the planned study.

12. Publication

It is planned to present the results of the clinical trial in a scientific journal or at a congress.

13. Sponsorship and conflict of interest

The investigator hereby declares that there are no agreements for sponsorship with the industry for the conduct of the present trial. Thus, there is no conflict of interest for the physicians involved in the study.

14. Amendments

Any change to the study protocol will be substantiated and documented. The changes are considered part of the study protocol.

15. Literature

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16. Responsibilities

Ronald Seidel, MD Principal investigator

Katharina Zukowski, MD Investigator

17. Attachements

Attachement 1 Informed Consent Form

Attachement 2 Case Report Form